```
=> fil reg
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  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> e prostanoid/cn
E1            1      PROSTANOIC ACID, 13,14-DIDEHYDRO-9,15-DIDEOXY-/CN
E2            1      PROSTANOIC ACID, 9.BETA.,11.ALPHA.,15-TRIHYDROXY-, MET
                     HYL ESTER, (15R)-/CN
E3            0 --> PROSTANOID/CN
E4            1      PROSTANOID FP RECEPTOR (HUMAN CLONE MKXR2)/CN
E5            1      PROSTANOID IP RECEPTOR (HUMAN CLONE 11/6HLXR3)/CN
E6            1      PROSTANOIDS/CN
E7            1      PROSTANOYL CARNITINE/CN
E8            1      PROSTANTHEROL/CN
E9            1      PROSTAPHILIN A/CN
E10           1      PROSTAPHLIN/CN
E11           1      PROSTAPHLIN A/CN
E12           1      PROSTAPHLYN/CN

=> s prostanoid?/cn
L1            3 PROSTANOID?/CN

=> s ?prostanoid?/cns
L2            3 ?PROSTANOID?/CNS
```

Searched by: Mary Hale 308-4258

MOHAMED
304147

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=> fil ca,capre,caplus,.biotech,wpids,uspatful
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=> s (l1 or l2 or prostanoid?)
L3         3286 FILE CA
L4           16 FILE CAPREVIEWS
L5         3303 FILE CAPLUS
L6         3522 FILE BIOSIS
L7         2847 FILE MEDLINE
L8         3107 FILE EMBASE
TRUNCATION SYMBOL NOT VALID AT BEGINNING OF '?PROSTANOID?'
L9          304 FILE USPATFULL

TOTAL FOR ALL FILES
L10      16385 (L1 OR L2 OR PROSTANOID?)
The truncation symbols #, ? and ! cannot be used at the beginning of
a search term.  If you are searching in a field that uses implied
proximity, and you used a truncation symbol after a punctuation mark,
the system may interpret the truncation symbol as being at the
beginning of a term.  Implied proximity is used in search fields
indexed as single words, for example, the Basic Index.

=> fil reg
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TSCA INFORMATION NOW CURRENT THROUGH DECEMBER 1995
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Searched by: Mary Hale 308-4258

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```
=> e noncyclooxygenase/cn
E1            1      NONCRON/CN
E2            1      NONCRON 60K/CN
E3            0 --> NONCYCLOOXYGENASE/CN
E4            1      NONDEZINC SM/CN
E5            1      NONDEZINC SMH/CN
E6            1      NONEMIC/CN
E7            1      NONEN-1-AMINIUM, N,N-DIMETHYL-N-(5,5,7,7-TETRAMETHYL-2
                     -OCTENYL)-, CHLORIDE/CN
E8            1      NONEN-1-OL, ACETATE/CN
E9            1      NONEN-1-OL, DIHYDROGEN PHOSPHATE/CN
E10           1      NONEN-1-OL, DIHYDROGEN PHOSPHATE, COMPD. WITH 2,2',2''
                     -NITRILOTRIS(ETHANOL)/CN
E11           1      NONEN-1-OL, HEPTADECAFLUORO-/CN
E12           1      NONEN-1-OL, HYDROGEN PHOSPHATE/CN

=> fil ca,capre,caplus,.biotech,wpids,uspatful
FILE 'CA' ENTERED AT 10:39:11 ON 21 MAY 96
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FILE 'CAPREVIEWS' ENTERED AT 10:39:11 ON 21 MAY 96
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=> s l10 and noncyclooxygenase?
L11           7 FILE CA
L12           0 FILE CAPREVIEWS
L13           7 FILE CAPLUS
L14           5 FILE BIOSIS
L15           5 FILE MEDLINE
L16           4 FILE EMBASE
TRUNCATION SYMBOL NOT VALID AT BEGINNING OF '?PROSTANOID?'
```

Searched by: Mary Hale 308-4258

L17 0 FILE USPATFULL

TOTAL FOR ALL FILES
L18 28 L10 AND NONCYCLOOXYGENASE?
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=> dup rem l18
PROCESSING COMPLETED FOR L18
L19 8 DUP REM L18 (20 DUPLICATES REMOVED)

=> d 1-8 an .mh

L19 ANSWER 1 OF 8 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 1
AN 96:131817 BIOSIS
TI 8-epi-PGF-2alpha, a novel **noncyclooxygenase**-derived prostaglandin, constricts airways in vitro.
SO American Journal of Respiratory and Critical Care Medicine 153 (2). 1996. 590-596. ISSN: 1073-449X
AU Kawikova I; Barnes P J; Takahashi T; Tadjkarimi S; Yacoub M H; Belvisi M G
AB 8-Epi-prostaglandin F-2alpha (8-epi-PGF-2alpha) is an F-2-isoprostane formed via a **noncyclooxygenase** pathway. We investigated whether 8-epi-PGF-2alpha has any effects on isolated guinea-pig and human airway smooth-muscle tone, and characterized the receptor involved in these effects. Cumulative concentration responses to 8-epi-PGF-2alpha in the absence or presence of **prostanoid** TP- and EP-1-receptors antagonists (ICI 192,605 and AH 6809, respectively) were compared with the responses to U46619 (a thromboxane A-2 mimetic) and PGF-2alpha. 8-epi-PGF-2alpha contracted airway smooth muscle with a rank order of potency of U46619 gt PGF-2alpha gt 8-epi-PGF-2alpha for guinea pig and U46619 gt 8-epi-PGF-2alpha gt PGF-2alpha for human smooth muscle. ICI 192,605 inhibited guinea-pig tracheal contraction produced by U46619 (pA-2 = 10.0) with a similar potency to its inhibition of the contraction induced by 8-epi-PGF-2alpha (apparent pK-B = 10.2, 10.3), but not that induced by PGF-2alpha (apparent pK-B = 6.6). AH 6809 inhibited contraction induced by PGF-2alpha (pA-2 = 6.6) with a greater potency than contraction induced by U46619 (apparent pK-B = 5.1, 5.2) or 8-epi-PGF-2alpha (apparent pK-B = 5.3). In human airways, ICI 192,605 inhibited contraction induced by U46619 and 8-epi-PGF-2alpha with apparent pK-B values of 9.5 and 9.4, respectively, and AH 6809 inhibited contraction induced by 8-epi-PCF-2alpha With apparent pK-B values of 5.7 and 5.4. We conclude that 8-epi-PGF-2alpha contracts human and guinea-pig airways via **prostanoid** TP receptors. However, if 8-epi-PGF-2alpha is formed in asthma, its production, unlike that of other **prostanoids**, would not be inhibited by cyclooxygenase inhibitors.

L19 ANSWER 2 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 2
AN 121:55061 CA

TI Plasma levels of a novel **noncyclooxygenase**-derived **prostanoid** (8-isoprostane) correlate with severity of liver injury in experimental alcoholic liver disease
SO J. Pharmacol. Exp. Ther. (1994), 269(3), 1280-5
CODEN: JPETAB; ISSN: 0022-3565
AU Nanji, Amin A.; Khwaja, Shamsuddin; Tahan, Steven R.; Sadrzadeh, S. M. Hossein
PY 1994
AB The authors used the intragastric feeding rat model for alc. liver disease to investigate the relationship between pathol. severity and lipid peroxidn. Lipid peroxidn. was assessed by measurement, in plasma, of a novel **noncyclooxygenase**-derived **prostanoid** (8-isoprostane). Six groups of animals fed ethanol and different dietary fats (satd. fat, corn oil and fish oil) were sacrificed at 1 mo. Histol. liver examn., plasma measurements of 8-isoprostane and measurements of microsomal conjugated dienes were carried out. Animals fed fish oil and ethanol developed the most severe liver injury and had the highest 8-isoprostane levels in plasma (919 .+-. 112 pg/mL). These levels were significantly higher than the levels seen in the corn oil-ethanol (498 .+-. 105 pg/mL) ($P < .02$) and satd. fat-ethanol (28.6 .+-. 11.8 pg/mL) ($P < .001$) groups. Rats fed satd. fat and dextrose and corn oil and dextrose had levels of < 20 pg/mL. However rats fed fish oil and dextrose had, on av., 8-isoprostane levels about 100-fold higher than those seen in the satd. fat-dextrose and corn oil-dextrose groups. A significant correlation between pathol. severity and plasma 8-isoprostane levels was seen in the fish oil ($r = 0.92$, $P < .--1$) and non-fish oil-treated groups ($r = 0.94$, $P < .001$). A significant correlation also was seen between 8-isoprostane levels and liver microsomal conjugated dienes ($r = 0.93$, $P < .001$). The authors' results provide strong support for the hypothesis that lipid peroxidn. in ethanol-fed rats contributes to pathol. liver injury.

L19 ANSWER 3 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 3
AN 119:157646 CA
TI Marked overproduction of non-cyclooxygenase derived **prostanoids** (F2-isoprostanes) in the hepatorenal syndrome
SO J. Lipid Mediators (1993), 6(1-3), 417-20
CODEN: JLMEEG; ISSN: 0921-8319
AU Morrow, Jason D.; Moore, Kevin P.; Awad, Joseph A.; Ravenscraft, Mark D.; Marini, Gianluigi; Badr, Kamal F.; Williams, Roger; Roberts, L. Jackson, II
PY 1993
AB In spite of extensive searching for clues to the pathogenesis of the hepatorenal syndrome (HRS), its cause remains an enigma. The renal dysfunction in HRS has been attributed to intense but reversible renal vasoconstriction. This has engendered the hypothesis that the renal vasoconstriction is caused by a circulating factor. Patients with HRS exhibit chronic endotoxemia and may have tissue hypoxia, an environment conducive for the formation of free radicals. Recently, the authors discovered a series of novel prostaglandin (PG) F2-like compds., termed F2-isoprostanes, that are produced in vivo as products of free radical catalyzed lipid peroxidn. independent of the cyclooxygenase enzyme. One of these compds, 8-epi-PGF2.alpha.,

has been found to be an extremely potent renal vasoconstrictor. Therefore, the authors quantified levels of these **prostanoids** in patients with HRS and compared them to various control groups. Plasma levels of these compds. were markedly elevated only in patients with HRS (113 pg/mL) compared to normal controls (19 pg/mL), patients with compensated liver disease (20 pg/mL), patients with decompensated liver disease (20 pg/mL), and patients with chronic renal failure (23 pg/mL). The increased levels of these compds. are unlikely the result of reduced hepatic and renal clearance of the compds. since levels are not markedly increased in patients with either decompensated liver disease or chronic renal failure alone. Whether F2-isoprostanes are the elusive mediators responsible for the renal vasoconstriction in HRS remains to be established. However, these findings do suggest that oxidant injury may be a fundamental abnormality involved in the pathogenesis of HRS.

L19 ANSWER 4 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 4
AN 118:120487 CA
TI Method and compositions to assess oxidative stress in vivo
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
IN Roberts, Jackson L.; Morrow, Jason D.
PI WO 9222668 A1 921223
AI WO 92-US4413 920527
PY 1992
AB The title method involves detn. of prostaglandin-type compds. and their metabolites produced by a **noncyclooxygenase** free radical-catalyzed mechanism. A mass spectroscopic assay for PGF2 compds. in urine is described; levels of individual compds. were in the range 500-3000 pg/mL.

L19 ANSWER 5 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 5
AN 117:84105 CA
TI Glomerular actions of a free radical-generated novel prostaglandin, 8-epi-prostaglandin F2.alpha., in the rat: evidence for interaction with thromboxane A2 receptors
SO J. Clin. Invest. (1992), 90(1), 136-41
CODEN: JCINAO; ISSN: 0021-9738
AU Takahashi, Kihito; Nammour, Tarek M.; Fukunaga, Megumu; Ebert, Joan; Morrow, Jason D.; Roberts, L. Jackson, II; Hoover, Richard L.; Badr, Kamal F.
PY 1992
AB 8-Epi-PGF2.alpha. and related compds. are novel **prostanoids** produced by a **noncyclooxygenase** mechanism involving lipid peroxidn. Renal ischemia-reperfusion injury increased urinary excretion of these compds. by 300% over baseline level. Intrarenal arterial infusion at 0.5, 1, and 2 .mu.g/kg per min induced dose-dependent redns. in glomerular filtration rate (GFR) and renal plasma flow, with renal function ceasing at the highest dose. Micropuncture measurements (0.5 .mu.g/kg per min) revealed a predominant increase in afferent resistance, resulting in a decrease in transcapillary hydraulic pressure difference, and leading to redns. in single nephron GFR and plasma flow. These changes were completely abolished or reversed by a TxA2 receptor antagonist, SQ

29,548. Competitive radioligand binding studies demonstrated that 8-epi-PGF2.alpha. is a potent competitor for [3H]SQ 29,548 binding to rat renal arterial smooth muscle cells (RASM) in culture. Furthermore, addn. of 8-epi-PGF2.alpha. to RASM or isolated glomeruli was not assocd. with stimulation of arachidonate cyclooxygenase products. Therefore, 8-epi-PGF2.alpha. is a potent preglomerular vasoconstrictor acting principally through TxA2 receptor activation. These findings may explain, in part, the beneficial effects of antioxidant therapy and TxA2 antagonism obsd. in numerous models of renal injury induced by lipid peroxidn.

L19 ANSWER 6 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 6
AN 115:150570 CA
TI Quantification of **noncyclooxygenase** derived **prostanoids** as a marker of oxidative stress
SO Free Radical Biol. Med. (1991), 10(3-4), 195-200
CODEN: FRBMEH; ISSN: 0891-5849
AU Morrow, Jason D.; Roberts, L. Jackson, II
PY 1991
AB A review with 12 refs. There is a unique class of prostaglandin F2-like compds. formed in vitro from arachidonyl-contg. lipids in plasma by a free radical-catalyzed mechanism. These **prostanoids** are also produced in vivo in humans by a similar **noncyclooxygenase** mechanism. Levels of these PGF2 compds. detected by a mass spectrometric assay in normal human blood plasma and urine range from 5-10 pg/mL and 500-3000 pg/mg creatinine, resp. Circulating levels of the compds. increase by as much as 200-fold in animal models of free radical-induced peroxidn. Quantification of these **prostanoids** by mass spectrometry may provide a new approach to assess oxidative stress in vivo in humans. A disadvantage of the assay is the potential of ex vivo formation of these compds. in biol. fluids contg. lipids. These compds. must be differentiated from PGF2 compds. that are formed via the cyclooxygenase enzyme. Because the levels of these compds. in normal human plasma and urine are relatively high, assays may be somewhat insensitive for the detection of increased prodn. at isolated sites of oxidant injury within the body, in which case sampling near localized sites of their formation may be required. There are obvious potential advantages assocd. with quantification of these novel products of lipid peroxidn. as a noninvasive approach to assess oxidative status in vivo in humans.

L19 ANSWER 7 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 7
AN 108:106914 CA
TI Endothelium-dependent relaxation of canine basilar arteries. Part 1: Difference between acetylcholine- and A 23187-induced relaxation and involvement of lipoxygenase metabolite(s)
SO Stroke (Dallas) (1987), 18(5), 932-7
CODEN: SJCCA7; ISSN: 0039-2499
AU Kanamaru, Kenji; Waga, Shiro; Kojima, Tadashi; Fujimoto, Kiyoshige; Ito, Hiroji
PY 1987
AB Vascular responses to acetylcholine (ACh) and the Ca2+ ionophore A 23187 were studied in rings of canine basilar arteries. In prepns. that were precontracted to a stable plateau by 3 .times. 10-6M

PGF2.alpha., 10-9-10-7M A 23187 elicited significant relaxation of the basilar arteries if the endothelium was intact. Judging from histol. findings, the ability of a ring to relax in this manner is due to the presence of the endothelium. The same concn. of A 23187 did not relax vascular tissues in which the endothelium was purposely disrupted. Although 10-7-10-3M ACh did not sufficiently produce endothelium-dependent relaxation of canine basilar artery rings, ACh in the same concn. did produce significant relaxation in canine femoral rings. Evidently, the sensitivity of the muscarinic receptor of cerebral arteries appears to be appreciably different from that of peripheral (femoral) arteries. Pretreatment with 1.5 .times. 10-5M indomethacin, a cyclooxygenase inhibitor, potentiated the contractile response produced by PGF2.alpha. in intact rings. Preincubation with the lipoxygenase inhibitors nordihydroguaiaretic acid at (NDGA) at 1.5 .times. 10-5M or AA861 at 10-5M prevented A 23187-induced relaxation. The same concn. of NDGA and AA861 did not affect endothelium-independent relaxation induced by glyceryl trinitrate. Endothelium-dependent relaxation of the canine basilar artery by A 23187 may be mediated by **noncyclooxygenase** metabolite(s).

L19 ANSWER 8 OF 8 CA COPYRIGHT 1996 ACS DUPLICATE 8
AN 105:203434 CA
TI Treatment with dexamethasone increases glomerular prostaglandin synthesis in rats
SO J. Pharmacol. Exp. Ther. (1986), 239(1), 296-301
CODEN: JPETAB; ISSN: 0022-3565
AU Erman, A.; Hassid, A.; Baer, P. G.; Nasjletti, A.
PY 1986
AB To det. whether chronic glucocorticoid excess influences the metab. of arachidonic acid [506-32-1] to prostaglandins (PGs) in the renal cortex, the effects of dexamethasone [50-02-2] (2.5 mg/kg/wk) on the metab. of arachidonic acid were examd. in renal cortex homogenates and microsomes and in isolated glomeruli. The the release of immunoreactive **prostanoids** from isolated glomeruli incubated for 30 min in buffered salt soln. at 37.degree. were also detd. Under basal conditions, glomeruli from dexamethasone-treated rats releeased .apprx.2-fold as much PGE2 [363-24-6] and PGF2.alpha. [551-11-1] as did glomeruli from vehicle-treated rats. During incubation with arachidonic acid (33 .mu.M) or Ca2+ ionophore, A23187 [52665-69-7] (2.0 .mu.g/mL), the release of PGE2 and PGF2.alpha. from glomeruli of rats receiving dexamethasone also exceeded the release from glomeruli of control rats. The rate of conversion of [1-14C]arachidonic acid to PGE2 and PGF2.alpha. and to less polar metabolites having the chromatog. mobility of 5-hydroxyeicosatetraenoic acid [71030-39-2] and 12-hydroxyeicosatetraenoic acid [71030-37-0], by isolated glomeruli and by renal cortex homogenates and microsomes from dexamethasone-treated rats, was higher than the conversions by control rats. The metab. of arachidonate was not inhibited by indomethacin (10 .mu.M), suggesting that it is not catalyzed by cyclooxygenase [39391-18-9]. Chronic dexamethasone treatment increases the release of glomerular PGE2 and PGF2.alpha. and the metabolic transformation of arachidonic acid by glomeruli and by renal cortex homogenates and microsomes via both cyclooxygenase and

noncyclooxygenase pathways.

```
=> s l10 and oxidative stress
L20          11 FILE CA
L21           0 FILE CAPREVIEWS
L22          11 FILE CAPLUS
L23           9 FILE BIOSIS
L24           9 FILE MEDLINE
L25          15 FILE EMBASE
TRUNCATION SYMBOL NOT VALID AT BEGINNING OF '?PROSTANOID?'
L26           0 FILE USPATFULL

TOTAL FOR ALL FILES
L27          55 L10 AND OXIDATIVE STRESS
The truncation symbols #, ? and ! cannot be used at the beginning of
a search term.  If you are searching in a field that uses implied
proximity, and you used a truncation symbol after a punctuation mark,
the system may interpret the truncation symbol as being at the
beginning of a term.  Implied proximity is used in search fields
indexed as single words, for example, the Basic Index.

=> s vivo and l27
L28           4 FILE CA
L29           0 FILE CAPREVIEWS
L30           4 FILE CAPLUS
L31           3 FILE BIOSIS
L32           2 FILE MEDLINE
L33           5 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
'CNS' IS NOT A VALID FIELD CODE
L34           1 FILE WPIDS
L35           0 FILE USPATFULL

TOTAL FOR ALL FILES
L36          19 VIVO AND L27

=> s l36 not l18
L37           2 FILE CA
L38           0 FILE CAPREVIEWS
L39           2 FILE CAPLUS
L40           3 FILE BIOSIS
L41           1 FILE MEDLINE
L42           4 FILE EMBASE
TRUNCATION SYMBOL NOT VALID AT BEGINNING OF '?PROSTANOID?'
L43           0 FILE USPATFULL

TOTAL FOR ALL FILES
L44          12 L36 NOT L18
The truncation symbols #, ? and ! cannot be used at the beginning of
a search term.  If you are searching in a field that uses implied
proximity, and you used a truncation symbol after a punctuation mark,
the system may interpret the truncation symbol as being at the
beginning of a term.  Implied proximity is used in search fields
indexed as single words, for example, the Basic Index.
```

=> dup rem l44
PROCESSING COMPLETED FOR L44
L45 6 DUP REM L44 (6 DUPLICATES REMOVED)

=> d an .mh 1-6

L45 ANSWER 1 OF 6 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 95269525 EMBASE
TI Excretion of F2-isoprostanes in bile: A novel index of hepatic lipid peroxidation.
SO Hepatology, (1995) 22/3 (962-968).
ISSN: 0270-9139 CODEN: HPTLD
AU Awad J.A.; Morrow J.D.
PY 1995
AB Lipid peroxidation is believed to be an important mechanism of liver injury caused by some xenobiotics. However, it has been difficult to demonstrate and quantify this process in **vivo**. Moreover, little is known about the disposition of lipids oxidized in the liver. F2-isoprostanes are **prostanoids** produced by nonenzymatic free radical-catalyzed peroxidation of arachidonic acid esterified to phospholipids. Hydrolysis of F2-isoprostanes from phospholipids by phospholipases yields free F2-isoprostanes. Excretion of F2-isoprostanes, both free and esterified to phospholipids, was measured in bile after administration of CCl4. The concentration of lipid-esterified F2-isoprostanes in bile exceeded that of free F2-isoprostanes. CCl4 caused a dose-dependent increase in biliary F2-isoprostane excretion that correlated better with the increase in liver F2-isoprostanes than it did with the increase in plasma F2-isoprostanes. Pretreatment with colchicine ameliorated CCl4-liver injury but did not affect baseline or CCl4-induced biliary F2-isoprostane excretion. Administration of diquat to selenium- deficient rats, which causes hepatic and renal necrosis, was associated with a 13-fold elevation of plasma F2-isoprostanes. However, both hepatic F2- isoprostane concentrations and biliary F2-isoprostane excretion were increased only threefold. These data suggest that quantification of F2-isoprostane excretion in bile may provide a sensitive and quantitative index of hepatic lipid peroxidation.

L45 ANSWER 2 OF 6 CA COPYRIGHT 1996 ACS DUPLICATE 1
AN 120:209308 CA
TI Formation of non-cyclooxygenase-derived **prostanoids** (F2-isoprostanes) in plasma and low density lipoprotein exposed to **oxidative stress** in vitro
SO J. Clin. Invest. (1994), 93(3), 998-1004
CODEN: JCINAO; ISSN: 0021-9738
AU Lynch, Sean M.; Morrow, Jason D.; Roberts, L. Jackson, II; Frei, Balz
PY 1994
AB F2-isoprostanes are PGF2-like compds. that are known to be formed in **vivo** by free radical oxidn. of arachidonyl-contg. lipids, and their plasma levels have been suggested as indicators of in **vivo oxidative stress**. As oxidn. of LDL, a likely causal factor in atherosclerosis, involves lipid peroxidn., the authors investigated whether F2-isoprotanes are

formed in plasma and LDL exposed to **oxidative stress**, and how F2-isoprostane formation is related to endogenous antioxidant status. In plasma exposed to aq. peroxyl radicals, lipid hydroperoxides and esterified F2-isoprostanes were formed simultaneously after endogenous ascorbate and ubiquinol-10 had been exhausted, despite the continued presence of urate, .alpha.-tocopherol, .beta.-carotene, and lycopene. In isolated LDL exposed to aq. peroxyl radicals or Cu2+, consumption of endogenous ubiquinol-10 and .alpha.-tocopherol was followed by rapid formation and subsequent breakdown of lipid hydroperoxides and esterified F2-isoprostanes, and a continuous increase in LDL's electronegativity, indicative of atherogenic modification. In Cu2+-exposed LDL, the decrease in esterified F2-isoprostane levels was paralleled by the appearance of free F2-isoprostanes, suggesting that hydrolysis by an LDL-assocd. activity had occurred. The authors' data suggest that F2-isoprostanes are useful markers of LDL oxidn. in **vivo**. As F2-isoprostanes are potent vascoconstrictors and can modulate platelet aggregation, their formation in LDL demonstrated here may also have important implications for the etiol. of cardiovascular disease.

L45 ANSWER 3 OF 6 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 93072955 EMBASE
TI Identification of non-cyclooxygenase-derived **prostanoid** (F2-isoprostane) metabolites in human urine and plasma.
SO J. BIOL. CHEM., (1993) 268/6 (4161-4169).
ISSN: 0021-9258 CODEN: JBCHA3
AU Awad J.A.; Morrow J.D.; Takahashi K.; Roberts L.J. II
PY 1993
AB Free radicals are thought to play an important role in many types of tissue injury. Recently, we reported that a series of prostaglandin F2-like compounds (F2-isoprostanes) capable of exerting potent biological activity are produced in **vivo** by free radical-induced lipid peroxidation. Their formation is independent of the cyclooxygenase enzyme and has been shown to increase profoundly in animal models of free radical injury and lipid peroxidation. We now report the identification of F-ring isoprostane metabolites in human urine and plasma utilizing a gas chromatographic/mass spectrometric assay for the major urinary metabolite of prostaglandin D2 (9.alpha.,11.beta.-dihydroxy-15-oxo-2,3,18,19-tetranorprost-5-ene-1,20-dioic acid). Evidence confirming these metabolites as tetranor, dicarboxylic acid compounds containing one double bond, cis-cyclopentane ring hydroxyls, and one keto group similar in structure to the major urinary metabolite of prostaglandin D2 was obtained by analysis of human urine by electron ionization mass spectrometry. Levels of these metabolites in normal human urine were determined and found to be unaffected by cyclooxygenase inhibitors. Evidence that these metabolites arise from F2-isoprostanes was obtained by demonstrating that (a) marked increases in plasma levels and urinary excretion of these metabolites, which were unaffected by coadministration of indomethacin, occurred in rats administered CCl4 to induce F2-isoprostane formation and (b) marked increases in levels of these metabolites in plasma and urine resulted from the intravenous infusion of F2-isoprostanes into a rat. Quantification of these

isoprostane metabolites in urine and plasma may provide a reliable index of endogenous isoprostane production which could prove to be an important advance in our ability to assess oxidant stress in **vivo** in humans.

L45 ANSWER 4 OF 6 BIOSIS COPYRIGHT 1996 BIOSIS
AN 93:96547 BIOSIS
TI NON-CYCLOOXYGENASE-DERIVED **PROSTANOIDS** F-2 ISOPROSTANES ARE FORMED IN-SITU ON PHOSPHOLIPIDS.
SO PROC NATL ACAD SCI U S A 89 (22). 1992. 10721-10728. CODEN: PNASA6 ISSN: 0027-8424
AU MORROW J D; AWAD J A; BOSS H J; BLAIR I A; ROBERTS L J II
AB We recently reported the discovery of a series of bioactive prostaglandin F2-like compounds (F2-isoprostanes) that are produced in **vivo** by free radical-catalyzed peroxidation of arachidonic acid independent of the cyclooxygenase enzyme. Inasmuch as phospholipids readily undergo peroxidation, we examined the possibility that F2-isoprostanes may be formed in situ on phospholipids. Initial support for this hypothesis was obtained by the finding that levels of free F2-isoprostanes measured after hydrolysis of lipids extracted from livers of rats treated with CCl4 to induce lipid peroxidation were more than 100-fold higher than levels in untreated animals. Further, increased levels of lipid-associated F2-isoprostanes in livers of CCl4-treated rats preceded the appearance of free compounds in the circulation, suggesting that the free compounds arose from hydrolysis of peroxidized lipids. This concept was supported by demonstrating that free F2-isoprostanes were released after incubation of lipid extracts with bee venom phospholipase A2 in vitro. When these lipid extracts were analyzed by HPLC, fractions that yielded large quantities of free F2-isoprostanes after hydrolysis eluted at a much more polar retention volume than nonoxidized phosphatidylcholine. Analysis of these polar lipids by fast atom bombardment mass spectrometry established that they were F2-isoprostane-containing species of phosphatidylcholine. Thus, unlike cyclooxygenase-derived prostandoids, F2-isoprostanes are initially formed in situ on phospholipids, from which they are subsequently released preformed, presumably by phospholipases. Molecular modeling of F2-isoprostane-containing phospholipids reveals them to be remarkably distorted molecules. Thus, the formation of these phospholipid species in lipid bilayers may contribute in an important way to alterations in fluidity and integrity of cellular membranes, well-known sequelae of oxidant injury.

L45 ANSWER 5 OF 6 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 2
AN 91:90182 BIOSIS
TI A SERIES OF PROSTAGLANDIN F-2-LIKE COMPOUNDS ARE PRODUCED IN-**VIVO** IN HUMANS BY A NON-CYCLOOXYGENASE FREE RADICAL-CATALYZED MECHANISM.
SO PROC NATL ACAD SCI U S A 87 (23). 1990. 9383-9387. CODEN: PNASA6 ISSN: 0027-8424
AU MORROW J D; HILL K E; BURK R F; NAMMOUR T M; BADR K F; ROBERTS L J II
AB Increasing attention has focused on the role of free radicals derived from oxygen in the pathophysiology of a wide variety of disorders. One of the well-recognized targets of free radical-induced injury is

peroxidation of lipids. Using a variety of approaches, we have found that a series of prostaglandin F2-like compounds are produced in **vivo** in humans by a non-cyclooxygenase mechanism involving free radical-catalyzed peroxidation of arachidonic acid. Levels of these compounds in normal human plasma and urine range from 5 to 40 pg/ml and 500 to 4000 pg/mg of creatinine, respectively. In rats, their formation was found to increase as much as 200-fold in association with marked free radical-catalyzed lipid peroxidation induced by administration of CCl4 and diquat. To explore whether these **prostanoids** can exert biological activity, the effects of one of the compounds formed by this mechanism, 8-epi-prostaglandin F2.alpha., was examined in the kidney in the rat. Infusion of 8-epi-prostaglandin F2.alpha. into a peripheral vein (5 .mu.g/kg per min) or intrarenally (0.5-2.0 .mu.g/kg per min) resulted in marked parallel reductions in renal blood flow and glomerular filtration rate. That the formation of these **prostanoids** is catalyzed by free radicals and that they can exert potent biological activity suggest that these **prostanoids** may participate as pathophysiological mediators in oxidant injury. Quantification of these compounds may also provide a noninvasive approach to assess oxidant status in humans. That the formation of these **prostanoids** occurs independent of the catalytic activity of the cyclooxygenase enzyme suggests that there may be limitations at times regarding the reliability of the use of cyclooxygenase inhibitors to assess the role of prostaglandins in certain pathophysiological processes.

L45 ANSWER 6 OF 6 CA COPYRIGHT 1996 ACS DUPLICATE 3
AN 115:86078 CA
TI Formation of unique biologically active prostaglandins in **vivo** by a non-cyclooxygenase free radical catalyzed mechanism
SO Adv. Prostaglandin, Thromboxane, Leukotriene Res. (1990), 21A(Prostaglandins Relat. Compd.), 125-8
CODEN: ATLRD6; ISSN: 0732-8141
AU Morrow, Jason D.; Hill, Kristina E.; Burk, Raymond F.; Nammour, Tarek M.; Badr, Kamal F.; Roberts, L. Jackson, II
PY 1990
AB Although the catalytic activity of the cyclooxygenase has been assumed obligatory for endogenous prostaglandin biosynthesis, these studies have elucidated that a series of novel biol. active prostaglandins are produced in **vivo** independent of cyclooxygenase activity. The discovery that the formation of these compds. is catalyzed by free radicals and that they can exert potent biol. activity provides the background and rationale for a new area for investigation into the possibility that these **prostanoids** may participate as mediators in the pathophysiol. of **oxidative stress** and injury.

=> s (biological fluid or plasma or cerebrospinal fluid or bile or lung lavage or lymph or joint fluid) and (oxidative stress or l1 or prostanoid? or noncyclooxygenase?)
L46 938 FILE CA
L47 23 FILE CAPREVIEWS
L48 970 FILE CAPLUS

Searched by: Mary Hale 308-4258

```
L49          982 FILE BIOSIS
L50          918 FILE MEDLINE
L51         1067 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
L52            3 FILE WPIDS
L53          180 FILE USPATFULL

TOTAL FOR ALL FILES
L54         5081 (BIOLOGICAL FLUID OR PLASMA OR CEREBROSPINAL FLUID OR BILE
                 OR LUNG LAVAGE OR LYMPH OR JOINT FLUID) AND (OXIDATIVE ST
                 RESS OR L1 OR PROSTANOID? OR NONCYCLOOXYGENASE?)

=> s l54 and vivo
L55          137 FILE CA
L56            4 FILE CAPREVIEWS
L57          139 FILE CAPLUS
L58          135 FILE BIOSIS
L59          122 FILE MEDLINE
L60          151 FILE EMBASE
L61            2 FILE WPIDS
L62          126 FILE USPATFULL

TOTAL FOR ALL FILES
L63          816 L54 AND VIVO

=> s l63 and (prostaglandin f2 or prostaglandin? )
L64           44 FILE CA
L65            0 FILE CAPREVIEWS
L66           44 FILE CAPLUS
L67           35 FILE BIOSIS
L68           48 FILE MEDLINE
L69           50 FILE EMBASE
L70            1 FILE WPIDS
L71           78 FILE USPATFULL

TOTAL FOR ALL FILES
L72          300 L63 AND (PROSTAGLANDIN F2 OR PROSTAGLANDIN? )

=> s (biological fluid or plasma or cerebrospinal fluid or bile or lung
lavage or lymph or joint fluid) and (oxidative stress and (l1 or
prostanoid? or noncyclooxygenase?))
L73            4 FILE CA
L74            0 FILE CAPREVIEWS
L75            4 FILE CAPLUS
L76            4 FILE BIOSIS
L77            3 FILE MEDLINE
L78            6 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
L79            1 FILE WPIDS
L80            0 FILE USPATFULL

TOTAL FOR ALL FILES
L81           22 (BIOLOGICAL FLUID OR PLASMA OR CEREBROSPINAL FLUID OR BILE
                 OR LUNG LAVAGE OR LYMPH OR JOINT FLUID) AND (OXIDATIVE ST
                 RESS AND (L1 OR PROSTANOID? OR NONCYCLOOXYGENASE?))
```

```
=> s l81 not (l18 or l36 or l44)
L82           1 FILE CA
L83           0 FILE CAPREVIEWS
L84           1 FILE CAPLUS
L85           1 FILE BIOSIS
L86           1 FILE MEDLINE
L87           1 FILE EMBASE
'L36' NOT FOUND
L88           0 FILE USPATFULL

TOTAL FOR ALL FILES
L89           5 L81 NOT (L18 OR L36 OR L44)

=> dup rem l89
PROCESSING COMPLETED FOR L89
L90            2 DUP REM L89 (3 DUPLICATES REMOVED)

=> d an .mh 1-2

L90  ANSWER 1 OF 2  CA  COPYRIGHT 1996 ACS              DUPLICATE 1
AN   124:7644  CA
TI   The influence of dietary fatty acids and Vitamin E on plasma
   prostanoids and liver microsomal alkane production in
     broiler chickens with regard to nutritional encephalomalacia
SO   J. Nutr. Sci. Vitaminol. (1995), 41(5), 553-61
     CODEN: JNSVA5; ISSN: 0301-4800
AU   Fuhrmann, Herbert; Sallmann, Hans-Peter
PY   1995
AB   Nutritional encephalomalacia (NE) in broiler chickens is considered
     as a peroxidative dysfunction caused by vitamin E-deficient diets.
     A feeding expt. was performed to investigate the consequences of
     feeding different fats in combination with increasing amts. of
     vitamin E on liver lipid peroxidn. and plasma
   prostanoid pattern. Newly hatched chicks from hens on a
     vitamin E-poor diet were fed with either mainly linolenic, linoleic
     or oleic acid-rich oils in a vitamin E-deficient (5 ppm) basic diet.
     The animals were supplemented with vitamin E on three levels (0, 20
     or 120 ppm). On appearance of the first symptoms of NE after 8 days
     post-hatching, the animals were examd. Typical symptoms with a high
     incidence only occurred in the group fed linoleic acid and 5 ppm
     vitamin E. Plasma prostanoids and microsomal
     alkane prodn. in liver as a measure of endogenous lipid peroxidn.
     were detd. The dietary conditions affected plasma
     prostaglandin E2 and thromboxane A2, but not prostacyclin. However,
     it seems unlikely that the prostanoids are involved in the
     pathogenesis of NE. Liver lipid peroxidn. increased in vitamin E
     deficiency. The level of alkanes depended on the type of fat
     supplied. The consequences of the different dietary fats in
     combination with vitamin E deficiency on peroxidative metab. of
     broiler chickens are evident, indicating that a high level of
   oxidative stress is imposed by the linoleic
     acid-rich fat.

L90  ANSWER 2 OF 2  MEDLINE                             DUPLICATE 2
```

AN 92119911 MEDLINE
TI The relationship of **oxidative stress** to thrombotic tendency in type 1 diabetic patients with retinopathy.
SO DIABETIC MEDICINE, (1991 Nov) 8 (9) 860-5.
Journal code: DME. ISSN: 0742-3071.
AU Jennings P E; McLaren M; Scott N A; Saniabadi A R; Belch J J
PY 1991
AB Increased free radical activity may contribute to thrombosis via effects on platelet aggregation and the **prostanoid** balance. To investigate this further we studied 15 Type 1 diabetic patients with retinopathy, matched with uncomplicated Type 1 patients for age, duration of diabetes and HbA1, together with matched healthy non-diabetic control subjects. The oxidative effects of free radicals as total diene conjugates and lipid peroxides were measured, together with redox status extracellularly as **plasma** albumin-thiols and intracellularly as erythrocyte superoxide dismutase activity. Platelet count, aggregation of platelets in whole blood to collagen, thromboxane B2, and prostacyclin stimulating factor (PGI2SF) were also assessed. Free radicals measured as lipid peroxides were significantly higher (9.6 (8.1-11.6) mumol l-1 (median and interquartile range) in diabetic patients with retinopathy than in control subjects (8.1 (7.4-9.2) mumol l-1; p less than 0.05). There were also significant reductions in redox status both extracellularly as **plasma** albumin thiols (408 (383-473) vs 490 (456-517) mumol l-1, p less than 0.001) and intracellularly as erythrocyte superoxide dismutase activity (34 (27-41) vs 44 (36-51) g l-1, p less than 0.05) between patients with retinopathy and control subjects. Platelet counts were increased in diabetic patients with retinopathy (p less than 0.05), as was collagen-induced platelet aggregation (p less than 0.01). Prostacyclin stimulating factor was reduced in patients with retinopathy (p less than 0.05) and correlated within the **plasma** with lipid peroxides (r = -0.53, p less than 0.04) and albumin thiols (r = 0.64, p less than 0.01). The results suggest that diabetic patients, particularly with retinopathy, are under **oxidative stress** and have an increased thrombotic tendency with increased platelet reactivity and a reduction in prostacyclin stimulating factor.

```
=> s roberts l?/au,in
L91          502 FILE CA
L92            2 FILE CAPREVIEWS
L93          505 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L94          833 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L95          746 FILE MEDLINE
'IN' IS NOT A VALID FIELD CODE
L96          488 FILE EMBASE
L97           79 FILE WPIDS
L98           97 FILE USPATFULL

TOTAL FOR ALL FILES
L99         3252 ROBERTS L?/AU,IN
```

Searched by: Mary Hale 308-4258

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=> s morrow j?/au,in
L100        334 FILE CA
L101          1 FILE CAPREVIEWS
L102        338 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L103        576 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L104        399 FILE MEDLINE
'IN' IS NOT A VALID FIELD CODE
L105        297 FILE EMBASE
L106         58 FILE WPIDS
L107         63 FILE USPATFULL

TOTAL FOR ALL FILES
L108       2066 MORROW J?/AU,IN

=> s l99 and l108
L109         40 FILE CA
L110          0 FILE CAPREVIEWS
L111         41 FILE CAPLUS
L112         62 FILE BIOSIS
L113         45 FILE MEDLINE
L114         33 FILE EMBASE
L115          0 FILE WPIDS
L116          0 FILE USPATFULL

TOTAL FOR ALL FILES
L117        221 L99 AND L108

=> s stress and l117
L118          8 FILE CA
L119          0 FILE CAPREVIEWS
L120          8 FILE CAPLUS
L121         13 FILE BIOSIS
L122          6 FILE MEDLINE
L123          8 FILE EMBASE
L124          0 FILE WPIDS
L125          0 FILE USPATFULL

TOTAL FOR ALL FILES
L126         43 STRESS AND L117

=> s l126 and  (l1 or prostanoid? or noncyclooxygenase?))
UNMATCHED RIGHT PARENTHESIS 'XYGENASE?))'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l126 and  (l1 or prostanoid? or noncyclooxygenase?)
L127          5 FILE CA
L128          0 FILE CAPREVIEWS
L129          5 FILE CAPLUS
L130          6 FILE BIOSIS
L131          4 FILE MEDLINE
L132          6 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
```

L133 0 FILE WPIDS
L134 0 FILE USPATFULL

TOTAL FOR ALL FILES
L135 26 L126 AND (L1 OR PROSTANOID? OR NONCYCLOOXYGENASE?)

=> dup rem l135
PROCESSING COMPLETED FOR L135
L136 9 DUP REM L135 (17 DUPLICATES REMOVED)

=> d 1-9 an .mhj
'.MHJ' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):an .mh

L136 ANSWER 1 OF 9 CA COPYRIGHT 1996 ACS DUPLICATE 1
AN 120:209308 CA
TI Formation of non-cyclooxygenase-derived **prostanoids** (F2-isoprostanes) in plasma and low density lipoprotein exposed to oxidative **stress** in vitro
SO J. Clin. Invest. (1994), 93(3), 998-1004
CODEN: JCINAO; ISSN: 0021-9738
AU Lynch, Sean M.; **Morrow, Jason D.; Roberts, L. Jackson, II**; Frei, Balz
PY 1994
AB F2-isoprostanes are PGF2-like compds. that are known to be formed in vivo by free radical oxidn. of arachidonyl-contg. lipids, and their plasma levels have been suggested as indicators of in vivo oxidative **stress**. As oxidn. of LDL, a likely causal factor in atherosclerosis, involves lipid peroxidn., the authors investigated whether F2-isoprotanes are formed in plasma and LDL exposed to oxidative **stress**, and how F2-isoprostane formation is related to endogenous antioxidant status. In plasma exposed to aq. peroxyl radicals, lipid hydroperoxides and esterified F2-isoprostanes were formed simultaneously after endogenous ascorbate and ubiquinol-10 had been exhausted, despite the continued presence of urate, .alpha.-tocopherol, .beta.-carotene, and lycopene. In isolated LDL exposed to aq. peroxyl radicals or Cu2+, consumption of endogenous ubiquinol-10 and .alpha.-tocopherol was followed by rapid formation and subsequent breakdown of lipid hydroperoxides and esterified F2-isoprostanes, and a continuous increase in LDL's electronegativity, indicative of atherogenic modification. In Cu2+-exposed LDL, the decrease in esterified F2-isoprostane levels was paralleled by the appearance of free F2-isoprostanes, suggesting that hydrolysis by an LDL-assocd. activity had occurred. The authors' data suggest that F2-isoprostanes are useful markers of LDL oxidn. in vivo. As F2-isoprostanes are potent vascoconstrictors and can modulate platelet aggregation, their formation in LDL demonstrated here may also have important implications for the etiol. of cardiovascular disease.

L136 ANSWER 2 OF 9 MEDLINE
AN 95126393 MEDLINE
TI Isoprostanes. Novel markers of endogenous lipid peroxidation and potential mediators of oxidant injury.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1994 Nov 15) 744 237-42. Ref: 17
Journal code: 5NM. ISSN: 0077-8923.
AU **Roberts L J 2nd; Morrow J D**
PY 1994
AB It was recently discovered that a series of structurally unique prostaglandin F2-like compounds (F2-isoprostanes) capable of exerting potent biological activity are produced in vivo in humans by a **noncyclooxygenase** mechanism involving free radical catalyzed peroxidation of arachidonic acid. Considerable evidence has been obtained suggesting that quantification of F2-isoprostanes represents an important advance in our ability to assess oxidant status in vivo in humans. This has allowed us to implicate oxidant **stress** in the pathogenesis of human disease-for example, the hepatorenal syndrome. In addition to the F2-isoprostanes, we recently discovered that E-ring and D-ring isoprostanes are also produced in abundance in vivo by rearrangement of the isoprostane endoperoxide intermediates. We have also been able to demonstrate that one of the E2-isoprostanes, 8-epi-PGE2, is a potent renal vasoconstrictor in the rat. Insights into factors that may influence the formation of E2/D2-isoprostanes relative to F2-isoprostanes should be important in advancing our understanding of the biological consequences of the formation of isoprostanes in vivo.

L136 ANSWER 3 OF 9 EMBASE COPYRIGHT 1996 ELSEVIER SCI. B.V.
AN 94158550 EMBASE
TI Mass spectrometry of **prostanoids**: F2-Isoprostanes produced by non- cyclooxygenase free radical-catalyzed mechanism.
SO METHODS ENZYMOL., (1994) 233/- (163-174).
ISSN: 0076-6879 CODEN: MENZAU
AU **Morrow J.D.; Roberts L.J. II**
PY 1994

L136 ANSWER 4 OF 9 CA COPYRIGHT 1996 ACS DUPLICATE 2
AN 118:184212 CA
TI Identification of non-cyclooxygenase-derived **prostanoid** (F2-isoprostane) metabolites in human urine and plasma
SO J. Biol. Chem. (1993), 268(6), 4161-9
CODEN: JBCHA3; ISSN: 0021-9258
AU Awad, Joseph A.; **Morrow, Jason D.**; Takahashi, Kihito; **Roberts, L. Jackson, II**
PY 1993
AB Recently, it was reported that a series of prostaglandin F2-like compds. (F2-isoprostanes) capable of exerting potent biol. activity are produced in vivo by free radical-induced lipid peroxidn. Their formation is independent of the cyclooxygenase enzyme and has been shown to increase profoundly in animal models of free radical injury and lipid peroxidn. This study reports the identification of F-ring isoprostane metabolites in human urine and plasma utilizing a gas chromatog./mass spectrometric assay for the major urinary metabolite of prostaglandin D2 (9.alpha.,11.beta.-dihydroxy-15-oxo-2,3,18,19-

tetranorprost-5-ene-1,20-dioic acid). Evidence confirming these metabolites as tetranor, dicarboxylic acid compds. contg. one double bond, cis-cyclopentane ring hydroxyls, and one keto group similar in structure to the major urinary metabolite of prostaglandin D2 was obtained by anal. of human urine by electro ionization mass spectrometry. Levels of these metabolites in normal human urine were detd. and found to be unaffected by cyclooxygenase inhibitors. Evidence that these metabolites arise from F2-isoprostanes was obtained by demonstrating that (a) marked increases in plasma levels and urinary excretion of these metabolites, which were unaffected by coadministration of indomethacin, occurred in rats administered CCl4 to induce F2-isoprostane formation and (b) marked increases in levels of these metabolites in plasma and urine resulted from the i.v. infusion of F2-isoprostanes into a rat. Quantification of these isoprostane metabolites in urine and plasma may provide a reliable index of endogenous isoprostane prodn. which could prove to be an important advance in our ability to assess oxidant **stress** in vivo in humans.

L136 ANSWER 5 OF 9 CA COPYRIGHT 1996 ACS DUPLICATE 3
AN 119:21041 CA
TI Airway and vascular effects of 8-epi-prostaglandin F2.alpha. in isolated perfused rat lung
SO J. Appl. Physiol. (1993), 74(1), 460-5
CODEN: JAPHEV; ISSN: 8750-7587
AU Kang, Kyung Ho; **Morrow, Jason D.; Roberts, L. Jackson, II**; Newman, John H.; Banerjee, Mukul
PY 1993
AB The effects of (8-epi-PGF2.alpha., a **noncyclooxygenase** free radical-catalyzed product of arachidonic acid, on pulmonary vascular and airway tone, its potency, and its mechanism of action were studied. Progressively increasing bolus doses (1.0, 5.0, 10.0, and 20.0 .mu.g) of 8-epi-PGF2.alpha. were injected into the pulmonary artery catheter of 18 isolated rat lungs, and a single dose (40.0 .mu.g) was injected into 7 addnl. rat lungs. The lungs were perfused with Krebs-Henseleit buffer soln. contg. 3% bovine serum albumin at 50 mL/kg/min during ventilation with 21% O2-5% CO2-74% N2. 8-Epi-PGF2.alpha. caused rapid pulmonary vascular and airway constrictor responses, which were followed by a gradual return over 10 min to baseline levels. Double vascular occlusion at peak rise in pulmonary arterial pressure (Ppa) revealed a 28% increase in arterial resistance. The rise in Ppa with 20 .mu.g of 8-epi-PGF2.alpha. was approx. 2-fold greater than with 20 .mu.g of the cyclooxygenase-derived prostaglandin PGF2.alpha.. The addn. of 100 .mu.M N-nitro-L-arginine, a blocker of endothelium-derived relaxing factor, in the perfusate potentiated the rise in Ppa by 244%. Injection of 40 .mu.g of rat atrial natriuretic factor at peak response to 20 .mu.g of 8-epi-PGF2.alpha. accelerated the return to baseline Ppa; it caused a 79% recovery in resistance to airflow across the lung and a 50% recovery in dynamic lung compliance values. Injection of 40 .mu.g of rat atrial natriuretic factor before 20 .mu.g of 8-epi-PGF2.alpha., on the other hand, caused 77 and 17% redns. in the rise in Ppa and lung resistance, resp., and an 8% redn. in the decline in dynamic compliance. Both the vascular and airway effects of 8-epi-PGF2.alpha. were fully

prevented by 40 .mu.M SQ 29548, a thromboxane receptor antagonist. Apparently, in rats, 8-epi-PGF2.alpha. is a modest vasoconstrictor of the pulmonary vasculature but a strong bronchoconstrictor. The mechanism of vaso- and bronchoconstriction appears to be due to the activation of thromboxane SQ 29548 receptors. 8-Epi-PGF2.alpha. may have important effects in the lungs during free radical **stress**.

L136 ANSWER 6 OF 9 BIOSIS COPYRIGHT 1996 BIOSIS
AN 93:96547 BIOSIS
TI NON-CYCLOOXYGENASE-DERIVED **PROSTANOIDS** F-2 ISOPROSTANES ARE FORMED IN-SITU ON PHOSPHOLIPIDS.
SO PROC NATL ACAD SCI U S A 89 (22). 1992. 10721-10728. CODEN: PNASA6 ISSN: 0027-8424
AU **MORROW J D**; AWAD J A; BOSS H J; BLAIR I A; **ROBERTS L J II**
AB We recently reported the discovery of a series of bioactive prostaglandin F2-like compounds (F2-isoprostanes) that are produced in vivo by free radical-catalyzed peroxidation of arachidonic acid independent of the cyclooxygenase enzyme. Inasmuch as phospholipids readily undergo peroxidation, we examined the possibility that F2-isoprostanes may be formed in situ on phospholipids. Initial support for this hypothesis was obtained by the finding that levels of free F2-isoprostanes measured after hydrolysis of lipids extracted from livers of rats treated with CCl4 to induce lipid peroxidation were more than 100-fold higher than levels in untreated animals. Further, increased levels of lipid-associated F2-isoprostanes in livers of CCl4-treated rats preceded the appearance of free compounds in the circulation, suggesting that the free compounds arose from hydrolysis of peroxidized lipids. This concept was supported by demonstrating that free F2-isoprostanes were released after incubation of lipid extracts with bee venom phospholipase A2 in vitro. When these lipid extracts were analyzed by HPLC, fractions that yielded large quantities of free F2-isoprostanes after hydrolysis eluted at a much more polar retention volume than nonoxidized phosphatidylcholine. Analysis of these polar lipids by fast atom bombardment mass spectrometry established that they were F2-isoprostane-containing species of phosphatidylcholine. Thus, unlike cyclooxygenase-derived prostandoids, F2-isoprostanes are initially formed in situ on phospholipids, from which they are subsequently released preformed, presumably by phospholipases. Molecular modeling of F2-isoprostane-containing phospholipids reveals them to be remarkably distorted molecules. Thus, the formation of these phospholipid species in lipid bilayers may contribute in an important way to alterations in fluidity and integrity of cellular membranes, well-known sequelae of oxidant injury.

L136 ANSWER 7 OF 9 CA COPYRIGHT 1996 ACS DUPLICATE 4
AN 115:150570 CA
TI Quantification of **noncyclooxygenase** derived **prostanoids** as a marker of oxidative **stress**
SO Free Radical Biol. Med. (1991), 10(3-4), 195-200 CODEN: FRBMEH; ISSN: 0891-5849
AU **Morrow, Jason D.**; **Roberts, L. Jackson, II**
PY 1991

AB A review with 12 refs. There is a unique class of prostaglandin F2-like compds. formed in vitro from arachidonyl-contg. lipids in plasma by a free radical-catalyzed mechanism. These **prostanoids** are also produced in vivo in humans by a similar **noncyclooxygenase** mechanism. Levels of these PGF2 compds. detected by a mass spectrometric assay in normal human blood plasma and urine range from 5-10 pg/mL and 500-3000 pg/mg creatinine, resp. Circulating levels of the compds. increase by as much as 200-fold in animal models of free radical-induced peroxidn. Quantification of these **prostanoids** by mass spectrometry may provide a new approach to assess oxidative **stress** in vivo in humans. A disadvantage of the assay is the potential of ex vivo formation of these compds. in biol. fluids contg. lipids. These compds. must be differentiated from PGF2 compds. that are formed via the cyclooxygenase enzyme. Because the levels of these compds. in normal human plasma and urine are relatively high, assays may be somewhat insensitive for the detection of increased prodn. at isolated sites of oxidant injury within the body, in which case sampling near localized sites of their formation may be required. There are obvious potential advantages assocd. with quantification of these novel products of lipid peroxidn. as a noninvasive approach to assess oxidative status in vivo in humans.

L136 ANSWER 8 OF 9 BIOSIS COPYRIGHT 1996 BIOSIS DUPLICATE 5
AN 91:90182 BIOSIS
TI A SERIES OF PROSTAGLANDIN F-2-LIKE COMPOUNDS ARE PRODUCED IN-VIVO IN HUMANS BY A NON-CYCLOOXYGENASE FREE RADICAL-CATALYZED MECHANISM.
SO PROC NATL ACAD SCI U S A 87 (23). 1990. 9383-9387. CODEN: PNASA6 ISSN: 0027-8424
AU **MORROW J D**; HILL K E; BURK R F; NAMMOUR T M; BADR K F; **ROBERTS L J II**
AB Increasing attention has focused on the role of free radicals derived from oxygen in the pathophysiology of a wide variety of disorders. One of the well-recognized targets of free radical-induced injury is peroxidation of lipids. Using a variety of approaches, we have found that a series of prostaglandin F2-like compounds are produced in vivo in humans by a non-cyclooxygenase mechanism involving free radical-catalyzed peroxidation of arachidonic acid. Levels of these compounds in normal human plasma and urine range from 5 to 40 pg/ml and 500 to 4000 pg/mg of creatinine, respectively. In rats, their formation was found to increase as much as 200-fold in association with marked free radical-catalyzed lipid peroxidation induced by administration of CCl4 and diquat. To explore whether these **prostanoids** can exert biological activity, the effects of one of the compounds formed by this mechanism, 8-epi-prostaglandin F2.alpha., was examined in the kidney in the rat. Infusion of 8-epi-prostaglandin F2.alpha. into a peripheral vein (5 .mu.g/kg per min) or intrarenally (0.5-2.0 .mu.g/kg per min) resulted in marked parallel reductions in renal blood flow and glomerular filtration rate. That the formation of these **prostanoids** is catalyzed by free radicals and that they can exert potent biological activity suggest that these **prostanoids** may participate as pathophysiological mediators in oxidant injury. Quantification of these compounds may also provide a noninvasive approach to assess oxidant status in humans. That the formation of these

prostanoids occurs independent of the catalytic activity of the cyclooxygenase enzyme suggests that there may be limitations at times regarding the reliability of the use of cyclooxygenase inhibitors to assess the role of prostaglandins in certain pathophysiological processes.

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TI Formation of unique biologically active prostaglandins in vivo by a non-cyclooxygenase free radical catalyzed mechanism
SO Adv. Prostaglandin, Thromboxane, Leukotriene Res. (1990), 21A(Prostaglandins Relat. Compd.), 125-8
CODEN: ATLRD6; ISSN: 0732-8141
AU **Morrow, Jason D.**; Hill, Kristina E.; Burk, Raymond F.; Nammour, Tarek M.; Badr, Kamal F.; **Roberts, L. Jackson, II**
PY 1990
AB Although the catalytic activity of the cyclooxygenase has been assumed obligatory for endogenous prostaglandin biosynthesis, these studies have elucidated that a series of novel biol. active prostaglandins are produced in vivo independent of cyclooxygenase activity. The discovery that the formation of these compds. is